

January 18, 1954

✓
1/19
Dear Ed:

To deal with constructive matters first, yes I'm happy to send you W-1305. ~~(under separate cover)~~. We have not manufactured an S^r derivative, but you should have no trouble in it. If you'd care to send such back, we might have some future use of it.

From the tone of your letter, I suppose you are already acquainted (whence?) with my reluctance to send out cultures that are the subject of instant study here. For some time, we had a completely unreserved policy, but the results worked out so badly that I am now adopting the alternative policy, though one which (as in the present case) it is sometimes rather embarrassing to uphold. To be consistent, I would have either to withhold a culture, or distribute it unreservedly. If you received material with strings attached, it would simply transfer to your own conscience the embarrassment of withholding it against forceful pressures. But if we can be of any other help to you, please let me know. Perhaps we could construct the diploids you were interested in? They are rather tricky beasts anyhow, whose behavior is full of pitfalls, so there might be some advantage to our keeping an eye on the genetic end of it. Or it may be that there are (not improbably) some inherent limitations that may not be immediately obvious but that would make a diploid analysis impractical. If I can consult with you on this, or assist in any other way, please let me know, as you can be sure that the notion of withholding materials, especially from my friends, is deeply distasteful to me and I would be looking for any alternative way of making it up.

Tom Nelson and I have been using the diploids to explore the details of elimination. In the first place it is clearly post-zygotic, (not pre-gametic), for the diploids in an $F^+ \times F^-$ cross are invariably hemizygous in the $Mal-S$ region, but not always for the contribution of the F^- parent. I.E., in about 85% of the diploids, the F^+ segment is missing; in about 12%, the F^+ segment is present and the F^- missing, and about 2% are crossovers, part F^- -type, part F^+ -type. This fits in very well with some data we have on segregational anomalies from an exceptional diploid once picked up which is in fact heterozygous for Mal and S , but appears to undergo elimination during segregation, so as to disturb the segregation ratios very markedly. These data were on numbers of haploid clones in single cell progenies, so relative growth does not come in. Finally, I've been pulling out the early hybrids as single cells by micromanipulation. In many instances, single cells have split out the full genotypes of the two parents, though the same cells show a restricted range of recombinants, i.e., with $Mal-S$ elimination usually of the F^+ (Hfr) contribution. Thus again

the timing of the defect can be narrowed to an event subsequent to the formation of the hybrid, but during or before segregation. The Het-diploids are clearly not the primary hybrids (if only because they can often be homozygous for some markers) but must be non-disjunctions of segregated meiotic products. The mating itself is probably a conjugation, with the F+ parent transferring a nucleus to the F- partner, but the cell studies are not yet absolutely conclusive on this. As you see, we are at a point of tying together a lot of loose ends to make a comprehensive picture, but I have not been moved to make too many explicit, public dicta on it until we are certain of our ground.

With best wishes to everyone,

Yours,

Joshua Lederberg

COPY